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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,326	04/03/2006	Yusuke Nakamura	082368-003000US	9667

20350 7590 02/01/2007

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EXAMINER
GUSSOW, ANNE

ART UNIT	PAPER NUMBER
1643	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/01/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/526,326	NAKAMURA ET AL.	
	Examiner	Art Unit	
	Anne M. Gussow	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-76* is/are pending in the application.

4a) Of the above claim(s) *1,5,6,8-35 and 37-76* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-4,7 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *February 28, 2005* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *April 3, 2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Sequence Alignment*.

DETAILED ACTION

1. Applicant's election with traverse of Group II, Claims 2-4, 7, and 36, and species CGX-2 (NFXL1) corresponding to SEQ ID Nos. 11 and 12 in the reply filed on December 6, 2006 is acknowledged. The traversal is on the ground(s) that NFXL1 (CGX-2, SEQ ID No. 12) is structurally different from the PNF1 protein of Peyman, et al. (cited in previous action) and that Groups I and II are properly related in that the polynucleotides of group II encode the polypeptides of group I as set forth in example 39 of the PCT International Search and Preliminary Examination Guidelines. This is not found persuasive because the PNF1 protein of Peyman, et al., as cited in the previous action, was found to be structurally similar to the protein of SEQ ID No. 4 and therefore unity of invention was found to be lacking.

In regards to the second part of applicant's argument, Example 39 of the PCT International Search and Preliminary Examination Guidelines continues past the segment cited in Applicant's response to discuss molecules which do not encode protein X of claim I and which hybridize to the protein of SEQ ID No. 2 (see PCT International Search and Preliminary Examination Guidelines page 98). The example states:

> "If an alternative DNA claim was presented that encompassed a DNA molecule that did not encode protein X, some Authorities might find that the claims did not share the same or corresponding technical feature and therefore lacked unity."

Claims 1c and 7 are drawn to molecules that hybridize to a sequence. Therefore, lack of unity is present and the restriction requirement is still deemed proper and is made FINAL.

2. The species of CGX-2 (NFXL1, SEQ ID No. 11 and 12) is free of the art, therefore, species CGX-3 (C20orf20, SEQ ID No. 3 and 4) is also under examination.

3. Claims 1, 5, 6, 8-35, 37-76 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on December 6, 2006.

4. Claims 2-4, 7, and 36 are under examination.

Drawings

5. The drawings are objected to because in Figure 20A the two Bromo domains are spelled "Brono". Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the

replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

6. The disclosure is objected to because of the following informalities: There are typographical and grammatical errors in the specification. For example, on page 13 line 8 interact should read "interacts", on page 15 line 28 it is unclear which gastric-cancer associated gene is being referred to and on page 19 line 22 bellow should be "below".

Appropriate correction is required throughout.

7. The use of the trademarks Matchmaker™, HybriZAP™, Herceptin™, Gleevec™, Iressa™, Ampliscribe™, ArrayVision™, Trizol™, Rneasy™, Superscript™, and Lipofectin™ have been noted in this application. They should be capitalized wherever they appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

8. Claims 2-4 and 7 are objected to because of the following informalities: Claim 2 refers to a non-elected claim, for this office action the limitations of the polynucleotide encoding the polypeptide of claim 1 will be read into the examined claims. Appropriate correction is required.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 2-4 and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, because it depends on claim 1.

The claim is drawn to a polynucleotide of claim 1 encoding a polypeptide that has a "biological activity equivalent" to a protein consisting of the amino acids sequence of any one of SEQ ID Nos. 2, 4, 6, 8, 10, and 12. It is not clear what biological activity equivalent is. Is it enzymatic activity, binding, activating, or inhibiting, for example?

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 2-4 and 7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polynucleotide encoding the polypeptide of SEQ ID Nos. 2, 4, 6, 8, 10, and 12, does not reasonably provide enablement for substitutions, deletions, insertions or additions to the sequences. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Claim is rejected because it is dependent upon claim 1. Claim 1b is broadly drawn to a polynucleotide that encodes a polypeptide comprising the amino acid sequence of SEQ ID Nos. 2, 4, 6, 8, 10, and 12 in which one or more amino acids are substituted, deleted, inserted, and/or added. Claim 1c is drawn to a polypeptide encoded by a polynucleotide that hybridizes under stringent conditions to a polynucleotide consisting of the nucleotide sequence of SEQ ID Nos. 1, 3, 5, 7, 9, and 11 wherein the polypeptide has a biological activity equivalent to a polypeptide consisting of the amino acid of any one of SEQ ID Nos. 2, 4, 6, 8, 10 and 12.

The specification discloses proteins ARHCL1 (CGX1, SEQ ID No. 2), NFXL1 (CGX2, SEQ ID No. 12), C20orf20 (CGX3, SEQ ID No. 4), LEMD1 (CGX4, SEQ ID Nos. 8 and 10), CCPUCC1 (CGX5, SEQ ID No. 6), Ly6E (CGX6), Nkd1 (CGX7), and LAPTM4beta (CGX8), which exhibit increased expression in colorectal cancers. The

specification does not disclose substitutions, deletions, insertions or additions to the sequences of these proteins.

Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, the replacement of a single lysine at position 118 of the acidic fibroblast growth factor by a glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (see Burgess et al, Journal of Cell Biology Vol 111 November 1990 2129-2138). In transforming growth factor alpha, replacement of aspartic acid at position 47 with asparagine, did not affect biological activity while the replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (see Lazar et al Molecular and Cellular Biology Mar 1988 Vol 8 No 3 1247-1252).

Replacement of the histidine at position 10 of the B-chain of human insulin with aspartic acid converts the molecule into a superagonist with 5 times the activity of nature human insulin. Schwartz et al, Proc Natl Acad Sci USA Vol 84:6408-6411 (1987). Removal of the amino terminal histidine of glucagon substantially decreases the ability of the molecule to bind to its receptor and activate adenylate cyclase. Lin et al Biochemistry USA Vol 14:1559-1563 (1975).

These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of the protein. Additionally, the polynucleotide that hybridizes to a polynucleotide of SEQ ID Nos. 1, 3, 5, 7, 9, or 11 would not encode the same protein as SEQ ID Nos. 2, 4, 6, 8, 10, or 12, nor have the same biological activity as the

complementary polynucleotide because the complementary polypeptide is not the coding strand of DNA.

Although biotechnology has made great strides in the recent past, these references serve to demonstrate exactly how little we really know about the art. The results of the construction of synthetic proteins remain very unpredictable as Burgess, et al., Lazar, et al., Schwartz, et al., and Lin, et al. conclusively demonstrate.

In view of the lack of guidance, lack of examples, and lack of predictability associated with regard to producing and using the myriad of derivatives encompassed in the scope of the claims, one skilled in the art would be forced into undue experimentation in order to practice the broadly claimed invention.

Claim Rejections - 35 USC § 101

13. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

14. Claim 7 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claim as written does not sufficiently distinguish over polynucleotides as they exist naturally because claim 7 does not particularly point out any non-naturally occurring differences between the claimed polynucleotide and the structure of a naturally occurring polynucleotide.

In the absence of the hand of man, the naturally occurring polynucleotide is considered non-statutory subject matter (Diamond v. Chakrabarty, 206 U.S.P.Q. 193 (1980)). It should be noted that the mere purity of a naturally occurring product does not necessarily impart patentability (Ex parte Siddiqui, 156 U.S.P.Q. 426 (1966)). However, when purification results in a new utility, patentability is considered (Merck Co. v. Chase Chemical Co., 273 F.Supp 68 (1967), 155 USPQ 139, (District Court, New Jersey, 1967)). Amendment of the claims to recite "an isolated" or "purified" polynucleotide or similar language would obviate this rejection.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

16. Claims 2-4, 7 and 36 are rejected under 35 U.S.C. 102(a,e) as being anticipated by Tang, et al. (WO 02/22660A2, published March 21, 2002).

The claims are drawn to an isolated polynucleotide encoding a polypeptide of SEQ ID No. 4 (CGX-3), a vector and host cell comprising the polynucleotide, a polynucleotide that is complementary to the polynucleotide or to the complementary

strand of the polynucleotide comprising at least 15 nucleotides, and a kit comprising a detection reagent which binds to one or more nucleic acid sequences selected from the group consisting of the CGX1-7 proteins (SEQ ID Nos. 2, 4, 6, 8, 10, or 12).

Tang, et al. teach an isolated polynucleotide 100% identical to SEQ ID No. 4. (See attached sequence alignment), an expression vector comprising the polynucleotide, a host cell comprising the polynucleotide, a polynucleotide comprising the complementary sequences (claims 1-9), and a kit comprising polynucleotide probes for detecting polynucleotides or polypeptides (page 5, 1st 2 paragraphs).

"Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Since the claims do not define the specific nucleotides of the complementary sequence and a 100% identical amino acid sequence would encode the same polypeptide and because of the indefinite nature of the biological activity (see 112 2nd paragraph, above), all the limitations of the claims have been met.

17. Claims 2-4, 7, and 36 are rejected under 35 U.S.C. 102(e) as being anticipated by Tang, et al. (WO 02/22660A2, priority date September 10, 2000).

The claims have been described supra.

Tang, et al. has been described supra.

Since the claims do not define the specific nucleotides of the complementary sequence and a 100% identical sequence would encode the same polypeptide and because of the indefinite nature of the biological activity (see 112 2nd paragraph, above), all the limitations of the claims have been met.

Conclusion

18. No claims are allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne M. Gussow whose telephone number is (571) 272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anne M. Gussow

January 23, 2007

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER

<!--StartFragment-->RESULT 2
ABB97195
ID ABB97195 standard; protein; 204 AA.
XX
AC ABB97195;
XX
DT 28-JUN-2002 (first entry)
XX
DE Novel human protein SEQ ID NO: 463.
XX
KW Human; antianaemic; vulnerary; antiinflammatory; immunomodulator;
KW antiinfertility; cerebroprotective; cytostatic; rheumatic; gene therapy;
KW neuroprotective; antiparkinsonian; protein therapy; EST;
KW expressed sequence tag.
XX
OS Homo sapiens.
XX
PN WO200222660-A2.
XX
PD 21-MAR-2002.
XX
PF 10-SEP-2001; 2001WO-US026015.
XX
PR 11-SEP-2000; 2000US-00659671.
XX
PA (HYSE-) HYSEQ INC.
XX
PI Tang YT, Liu C, Zhou P, Asundi V, Zhang J, Zhao QA, Ren F;
PI Xue AJ, Yang Y, Wehrman T, Drmanac RT;
XX
DR WPI; 2002-292408/33.
DR N-PSDB; ABN32381.
XX
PT An isolated polynucleotide for treating diseases associated with its
PT encoded polypeptide such as cancer and multiple sclerosis.
XX
PS Example 2; SEQ ID NO 463; 509pp; English.
XX
CC The present invention provides the protein and coding sequences of 444
CC novel human proteins. These were isolated from expressed sequences tags
CC (ESTs). They can be used to stimulate cell growth, to regulate
CC haematopoiesis e.g. to treat aplastic anaemia, to help tissue regrowth
CC e.g. in burn treatment, to regulate the immune system e.g. to treat
CC multiple sclerosis, to regulate activin or inhibin e.g. to treat
CC infertility, to regulate haemostasis or thrombolysis e.g. to treat stroke
CC and cancer, to screen for drugs, to treat inflammatory conditions e.g.
CC rheumatoid arthritis, and to treat nervous system disorders e.g.
CC Parkinson's disease. The present sequence is a protein of the invention
XX
SQ Sequence 204 AA;

  Query Match   100.0%; Score 1067; DB 5; Length 204;
  Best Local Similarity   100.0%; Pred. No. 2.8e-103;
  Matches 204; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 MGEAEVGGGGAAGDKGPGEAATSPAEETVVWSPEVEVCLFHAMLGHKPVGVNRHFHMICI 60
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Qy   61 RDKFSQNIGRQVPSKVIWDHLSTMYDMQALHESEILPFPNPERNFVLPEEIIQEVREGKV 120
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               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         121 MIEEEMKEEMKEDVDPHNGADDVFSSSGSLGKASEKSSKDKEKNSSDLGCKEGADKRKRS 180

Qy         181 RVTDKVLTANSNPSSPSAAKRRRT 204
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Db         181 RVTDKVLTANSNPSSPSAAKRRRT 204

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